

## REMARKS

### CLAIM AMENDMENT

Claim 15 is amended into an independent version of claim 8 to pre-emptively avoid a possible section 112 rejection in view of the recent Federal Circuit decision *Pfizer v. Ranbaxy*.<sup>1</sup>

Applicant amends the independent claims to correct a typographical error and to conform the claims to the specification.

### SECTION 103 REJECTION OF CLAIMS 1, 8, AND 15

#### Combination of references fails to teach all limitations

*Basser*<sup>2</sup> fails to teach claim 1's limitation of "obtaining, from a *plurality* of test subjects, DT-MRI data from which an initial estimate of the tensor can be derived."

*Basser* teaches obtaining the diffusion tensor for a *single* test subject. Nowhere does *Basser* obtain data from a *plurality* of test subjects in an effort to provide an initial estimate of a *single* diffusion tensor (i.e. "the diffusion tensor" in claim 1).

The *deCharms*<sup>3</sup> publication teaches a biofeedback system. In a biofeedback system, such as that taught by *deCharms*, a subject observes his brain activity as he carries out a task. This enables the subject to adjust the way he carries out the task in an effort to make his brain activity conform to some desired brain activity.

The *deCharms* publication is entirely concerned with the brain activity of a *single person*. Therefore, *deCharms* teaches nothing about inter-subject variation of DT-MRI data from a plurality of subjects.

*DeCharms* allegedly teaches claim 1's limitations of determining values of intra-subject variation and inter-subject variation of DT-MRI data from a plurality of test subjects at

<sup>1</sup> *Pfizer v. Ranbaxy* 457 F.3d 1284 (Fed. Cir. 2006).

<sup>2</sup> *Basser*, US 5,539,310.

<sup>3</sup> *deCharms*, US 2002/0103428 (The Examiner has actually cited the patent that ultimately issued thereon but used paragraph numbers from the pre-grant publication to refer to specific passages. For consistency, Applicant refers to the pre-grant publication, which appears to be essentially identical to the issued patent.)

paragraphs 439, 449, 465, 471, 512, 600, and 645. It is therefore useful to examine each of these paragraphs carefully to learn what they disclose.

The first of the seven paragraphs, paragraph 439, reads as follows:

*"One type of pre-processing that may be performed on the input image/volume data may be spatial smoothing according to standard methods to produce smoothed image/volume output data. This is useful because it removes noise in the data, improves statistical properties by making the data variance more gaussian, and produces an image that is easier to interpret visually. This is accomplished by convolving the data with a 2-D or 3-D gaussian filter function with a defined half-width."*

Paragraph 439 therefore teaches that it is a good idea to smooth data that one has acquired from a subject and suggests a way to do so. The subject matter of paragraph 439 concerns only a single subject. It has nothing to do with determining separate first and second values indicative of intra-subject variation and inter-subject variation respectively.

The second of the seven paragraphs, paragraph 449, reads as follows:

*"Another type of pre-processing that may be performed on the input image/volume data may be motion correction to adjust for the motion that takes place between subsequent scans. This is useful because each section of each volume is in substantially the same position as in the first or reference scan of a scanning session. This can take place by applying using a transform created for each scan volume to that scan volume. The transform is designed to create the best fit in the least-squared error sense between the data of the current scan and the reference scan, including translation, rotation, and scaling if needed. An example of this software is described in: CC Lee, et al. Real-time adaptive motion correction in functional MRI. Magn Reson Med 1996;36:536-444 and in manuals and literature associated with existing MRI/MRI/PET data processing packages. Each of these steps, which can take place individually or in combination and in any order, will be familiar to one skilled in the art. These pre-processing steps may be applied to one or more reference scan, typically an early scan from the scanning session that will be used as a basis of comparison for computing activation images/volumes. These preprocessing steps may also be applied to each successive scan collected. The pre-processing for the reference scan(s) need not be the same as for subsequent scans. These pre-processing steps lead to pre-processed scan volumes for each sampled time point, which*

*are then used for further computation and processing. The use of motion correction software may be used to allow motion of the subject relative to the measurement apparatus while measurements are collected and/or training is conducted, those measurements being corrected so that voxels correspond to the appropriate locations within the brain of the subject."*

Paragraph 449 thus teaches that it is also a good idea to correct for motion that might occur between scans of the same subject. Once again, the subject matter of this paragraph concerns only a single subject. It has nothing to do with determining separate first and second values indicative of intra-subject variation and inter-subject variation respectively.

The third of the seven paragraphs, paragraph 465, reads as follows:

*"Another type of activation image/volume that may be computed is a variance image/volume. The variance of any pixel or group of pixels over a period of time can be computed, and these values can be formed into a variance image/volume. These images can be useful in located blood vessels, which might be excluded from further analysis in certain instances where brain matter physiology is the target, or focused upon if vascular perfusion is the target."*

Paragraph 465 thus teaches calculating the variance of a pixel over several scans of the same subject. Again, the subject matter of this paragraph concerns only a single subject. It has nothing to do with determining separate first and second values indicative of intra-subject variation and inter-subject variation respectively.

The fourth of the seven paragraphs, paragraph 471, reads as follows:

*"Another type of activation image/volume that may be computed is a thresholded map. Thresholds may be computed and used to cut out certain most relevant portions of the data from activation images/maps. Thresholds can be defined as a mean value of a region, or some fraction of the mean value. The fraction can be defined by a measure of the variance. An example threshold would be two standard deviations below the mean value of an entire activity pattern image. In some cases it may be helpful to set all values below or above a set threshold to a background level."*

Paragraph 471 thus teaches showing which pixels in an image have reached some threshold value. It also offers advice on how to calculate the threshold value. The variance referred to in paragraph 471 quantifies how much a pixel varies around some mean value of all pixels in the image.

The fifth of the seven paragraphs, paragraph 512, reads as follows:

*"As has been noted, an important aspect of the present invention relates to the provision of information to the subject as the subject's brain activity is measured in order to influence how the subject performs training exercises in one variation, information is communicated to the subject through computer generated displays which the subject is able to observe during training."*

Paragraph 512 thus describes how a biofeedback system works. It has nothing whatsoever to do with either inter-subject or intra-subject variation.

The sixth of the seven paragraphs, paragraph 600, reads as follows:

*"According to this variation, the voice of the subject is picked up using a microphone within the apparatus, transmitted, amplified, and played to the device operator or other healthcare professional, either nearby or distant. This recording can be turned off automatically or manually during the process of scanning. The voice of the device operator or other healthcare professional is picked up using a microphone, transmitted, amplified, and played to the subject. In some instances, one-way or two-way video communication is also used by imaging the patient in substantially real time and presenting the image to the device operator or other healthcare professional, or imaging the device operator or other healthcare professional and presenting the image to the subject in substantially real time on the monitor viewed by the subject."*

Paragraph 600 thus describes how the subject communicates with a device operator or a health-care professional during the biofeedback session. It clearly has nothing to do with inter-subject variation or intra-subject variation.

The last of the seven paragraphs, paragraph 645, reads as follows:

*"This invention may be used in conjunction with a variety of means for measuring physiological activity from a subject. Examples of measurement technologies include, but are not limited to, functional magnetic resonance imaging (fMRI), PET, SPECT, magnetic resonance angiography (MRA), diffusion tensor imaging (DTI), trans-cranial ultrasound and trans-cranial doppler shift ultrasound. It is anticipated that future technologies may be developed that also allow for the measurement of activity from localized brain regions, preferably in substantially real time. Once developed, these technologies may also be used with the current invention. These measurement techniques may also be used in combination, and in combination with other measurement techniques such as EEG, EKG, neuronal recording, local field potential recording, ultrasound, oximetry, peripheral pulse oximetry, near infrared spectroscopy, blood pressure recording, impedance [sic] measurements, measurements of central or peripheral reflexes, measurements of blood gases or chemical composition, measurements of temperature, measurements of emitted radiation, measurements of absorbed radiation, spectrophotometric measurements, measurements of central and peripheral reflexes, and anatomical methods including X-Ray/CT, ultrasound and others."*

This last paragraph enumerates the various ways one might measure brain activity. It has nothing to do with data processing steps that follow the collection of data about brain activity. In particular, it has nothing to do with determining separate first and second values indicative of intra-subject variation and inter-subject variation respectively..

It is abundantly clear that not even one of the seven paragraphs cited teaches the determination of separate first and second values indicative of intra-subject variation and inter-subject variation respectively.. Accordingly, even if one were to somehow combine *deCharms* with *Basser*, the result would still fail to teach all the limitations recited in the independent claims.

#### Motivation to combine references

As motivation to combine the references, the Examiner states that it would have been obvious to do so "to improve real time data improving data quality."

As an initial matter, it is unclear how combining the *Basser* and *deCharms* references would do anything at all to "improve real time data improving data quality." *Basser* teaches a

way to measure a diffusion tensor; *deCharms* teaches a biofeedback system. Neither reference has anything to do with real-time data acquisition.

Since neither reference raises the problem of real time data acquisition, Applicant submits that the idea of combining the references "to improve real time data improving data quality" may have been contrived in hindsight in an attempt to cobble together two references that allegedly teach all the claim limitations.

Claims 8 and 15 recite limitations similar to claim 1 and are therefore patentable for at least the same reasons. The remaining claims are dependent on one of claims 1, 8, and 15 and are therefore patentable for at least the same reasons.

#### **SECTION 103 REJECTION OF CLAIMS 2 AND 9**

Claim 2 recites the additional limitation of generating adjusted data by adjusting DT-MRI data by a subject specific additive offset determined on the basis of values indicative of inter-subject and intra-subject variation in DT-MRI data.

*Basser* allegedly teaches the additional limitation of generating "adjusted data" at col. 3 line 15 and at col. 3, lines 17-19. These two passages describe FIGS. 5A and 5B as depicting diffusion tensor ellipsoids from a pork loin. According to these passages, the difference between FIGS. 5A and 5B is a 40 degree rotation of a fiber axis.

Applicant suspects that the Examiner regards this 40 degree rotation as claim 1's additive offset, and that the rotation of the fiber axis in FIG. 5B amounts to claim 2's step of adjusting DT-MRI data by this 40 degree additive offset.

In fact, rotation of the fiber axis is not carried out by an additive offset. As one of ordinary skill in the art would realize, an additive offset results in *translation* of one coordinate system relative to the other, not rotation. One of ordinary skill in the art would know that rotation of a coordinate systems generally requires matrix *multiplication*, not an additive offset.

Moreover, claim 2 requires that any additive offset be "subject specific." There is nothing in *Basser* to suggest that the 40 degree rotation of the pork loin's diffusion tensor in FIG. 5B relative to FIG. 5A had anything to do with the particular subjects (i.e., the pigs) that donated the two pork loin. In fact, according to col. 16, lines 24-26, *Basser* uses the same pork loin for FIGS. 5A and 5B.

Accordingly, there is no basis for a section 103 rejection of claim 3 because even if one were to combine the references, there would still be no teaching of the additional limitation of claim 2. Claim 9 recites limitations similar to claim 2 and is patentable for at least the same reasons.

#### **SECTION 103 REJECTION OF CLAIMS 3 AND 10**

Claim 3 requires the additional limitation of generating a bowtie plot from DT-MRI data that has been adjusted by a subject specific additive offset determined on the basis of values indicative of inter-subject and intra-subject variation in DT-MRI data.

The Examiner suggests that generating a bowtie plot is taught in the same two passages described above in connection with claim 2. However, neither FIG. 5A nor 5B actually shows a bowtie plot.

Accordingly, there is no basis for a section 103 rejection of claim 3 because even if one were to combine the references, there would still be no teaching or suggestion of a bowtie plot. Claim 10 recites limitations similar to claim 3 and is patentable for at least the same reasons.

#### **SECTION 101 REJECTION OF CLAIMS 8-15**

The Examiner rejects claim 8 because it allegedly recites a data structure, and that under *In re Warmerdam*,<sup>4</sup> data structures are non-statutory.

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<sup>4</sup> *In re Warmerdam*, 33 F.3d 1354 (Fed. Cir. 1994).

The Examiner's reliance on *Warmerdam* is misplaced because claim 6 of *Warmerdam*'s application recited "A *data structure* generated by the method of any of claims 1 through 4." Thus, the preamble of *Warmerdam*'s claim 6 recited a data structure.

In contrast, claim 8's preamble does *not* recite a data structure as did *Warmerdam*'s claim 6. Applicant's claim 8 recites a computer-readable medium. A computer-readable medium is an article of manufacture, and is therefore well within the statutory subject matter defined by section 101. It is not a data structure.

Structurally, Applicant's claim 8 is similar to claim 1 of *In re Lowry*,<sup>5</sup> which recited "A memory for storing data for access by an application program being executed on a data processing system, comprising a data structure stored in said memory..."

In *Lowry*, the Court noted that the Board had reversed the Examiner's section 101 rejection of claim 1, stating that "[t]he Board found that claims 1 through 5, directed to a memory containing stored information, as a whole, recited an article of manufacture."

Applicant's claim 8, like the claim at issue in *Lowry*, recites an *article of manufacture*, and is therefore well within the scope of section 101. Accordingly, Applicant requests reconsideration and withdrawal of the section 101 rejection of claim 8, and all claims dependent thereon.

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<sup>5</sup> *In re Lowry* 32 F.3d 1579 (Fed. Cir. 1994).

**SUMMARY**

Now pending in this application are claims 1-15, of which claims 1, 8, and 15 are independent. No fees are believed to be due in connection with the filing of this amendment. However, to the extent fees are due, or if a refund is forthcoming, please adjust our deposit account no. 06-1050, referencing Attorney Docket No. 04843-046001.

Respectfully submitted,

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Faustino A. Lichauro  
Reg. No. 41,942

Fish & Richardson P.C.  
225 Franklin Street  
Boston, MA 02110  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906